a.) Amendment to the Specification

Please amend the paragraphs starting at page 1, line 8 and ending at page 3, line 1 to read as follows.

Migraine is a paroxysm of headache lasting 4 to 72 hours, which is accompanied by nausea, vomiting, extreme sensitivity to light and sound, and the like [Merck Manual, 17th Edition, Section 168; Therapeutic Guideline of Japanese Society of Neurology (Societas Neurologica Japonica); International Classification of Headache Disorders-II: ICHD-II, 2004]. As one of pathophysiology of migraine and the underlying mechanisms, vasodilation of extra- and/or intra-cranial blood vessels including superficial temporal artery has been proposed [Arch. Neurol. Psychiatr., vol.39, p.737-763 (1938); Cephalalgia, vol.1, p.143-147 (1981); Naika (Internal Medicine), vol.81, p.601-609 (1998); Naika, vol.81, p.639 (1998)]. It has also been known that the hydrophilic agonists of serotonin receptor 5-HT_1 (5-hydroxytryptamine 1) such as ergot alkaloid and sumatriptan, which poorly cross the blood brain barrier, are effective for the treatment of migraine since they can contract the dilated cranial blood vessels via the serotonin receptor 5-HT_1 of ~~cerebrovascular smooth muscle~~ cerebral artery [Ann. N.Y. Acad. Sci., vol. 600, p.587-600 (1990); Neurology, vol.43, p.S43-S47 (1993)].

Thus, it has been assumed that migraine could be treated by suppressing vasodilation of the extra- and/or intra-cranial blood vessels.

On the other hand, it has also been reported that the adenosine concentrations in the plasma of patients suffering from migraine are increased at an average of 68% at one hour after the migraine attack compared with those in crisis-free periods, that activation A_2 receptors by adenosine ~~reduces~~ causes a dose-dependent

serotonin uptake by platelets and consequently the vasodilation is induced by rapid ~~release~~ reduction of serotonine [Can. J. Neurol. Sci., vol.2, p.55-58 (1998)], and that intravenous injection of the adenosine potentiator to patients suffering from migraine induces the migraine attack [Med. J. Aust., vol.162, p.389-390 (1995)]. In addition, it has been known that adenosine has a potent vasodilating action and that an adenosine A_{2A} receptor and an adenosine A_{2B} receptor are involved in the vasodilation during the migraine attack and in the vasodilation induced by adenosine [Am. J. Physiol. Heart Circ. Physiol., vol.280, p.2329-2335 (2001)]. In view of these facts, it has been considered that migraine could be treated by suppression of vasodilation induced by adenosine.

Please amend the paragraphs starting at page 12, line 7 and ending at page 14, line 5 to read as follows.

The basilar (cerebral) arteries were removed and cut into rings segments of about 2 mm in width. Each ring segment was fixed with a silk thread to a needle cut into about 2 mm in length. The needle was attached to a holder provided in an Easy-Magnus System (Model no. UC-2; IWASHIYA KISHIMOTO MEDICAL INSTRUMENTS); the ring segments were immersed in a nutritive solution and allowed to stabilize at a resting tension of 0.2 g (1.96 mN) for more than 60 minutes. Into the organ bath (2 mL) of the Easy-Magnus System, the ~~cerebrovascular smooth muscle~~ cerebral artery was relaxed by application of 2 μL of 10 mmol/L adenosine aqueous solution. After that, the test compound was added cumulatively; 1 μL of 0.2 mmol/L dimethylsulfoxide solution, 1 μL of 0.4 mmol/L dimethylsulfoxide solution, and 0.7 μL of 2 mmol/L dimethylsulfoxide solution in order (Test compound-added group). Separately, in the same manner as in the

Test compound-added group, dimethylsulfoxide alone was cumulatively added in place of the test compound (Vehicle group). The contraction of the ~~cerebrovascular smooth muscle~~ cerebral artery was recorded on a recorder (Yokogawa) from an isometric force transducer (Nihon Kohden) connected to the holder, to which the ring was fixed, through a strain-pressure amplifier (Nihon Kohden).

The contractile effects were shown in Fig. 1 as a suppressive rate (%) of the test compound to the adenosine-induced relaxation of the cerebrovascular smooth muscle.

From the above results, the followings became clear.

The relaxation was recognized with addition of adenosine in the isolated ~~cerebrovascular smooth muscle~~ cerebral artery, and the adenosine-induced relaxation of the ~~cerebrovascular smooth muscle~~ cerebral artery was dose-dependently and significantly suppressed by addition of Compound 2, in comparison with the Vehicle group.